State of the Art and Science in Autism

Tina Iyama, M.D.

2007

Overview

- The clinical diagnosis autism
- The autism spectrum
- The causes of autism
- Medical Evaluation
- Early identification and intervention

Autism is a developmental disability that describes children who have difficulty with social and linguistic reciprocity and who have repetitive behaviors and a restricted range of interests.

Autism is an idea, a way of thinking about children with certain strengths and challenges.

Autism is a clinical impression. It is one facet of neurodevelopmental disorders.

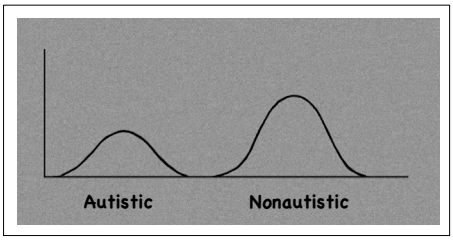
Children's brains are more complex than our diagnostic boxes.

Neurodevelopmental Disorders

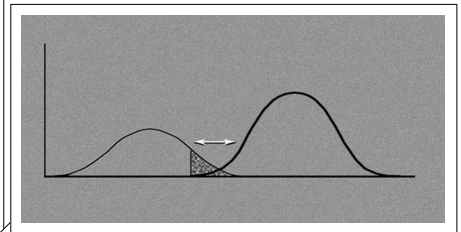
- Motor symptoms--->cerebral palsy
- Cognitive delays--->MR/CD/ID
- Social/comm problems--->autism
- Executive function def.--->ADHD
- Problems with one aspect of learning
  - ---->learning disability

There is no diagnostic truth.

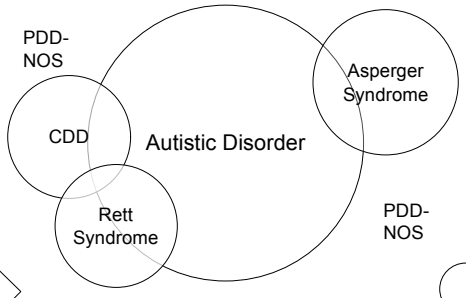
The Ideal World



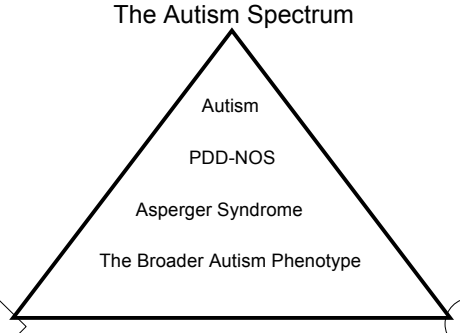
The Real World



Current conceptualization



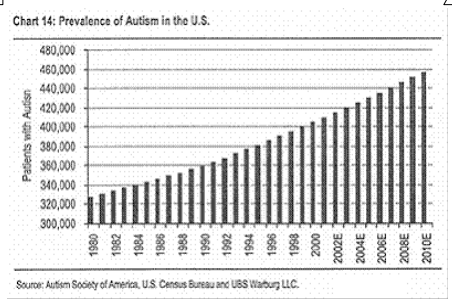
The Autism Spectrum

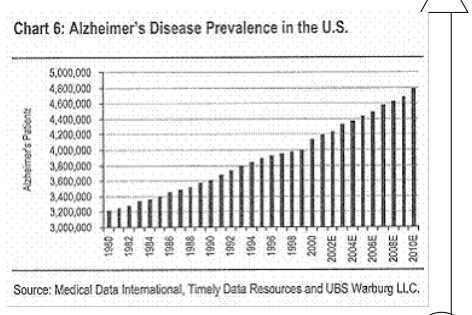


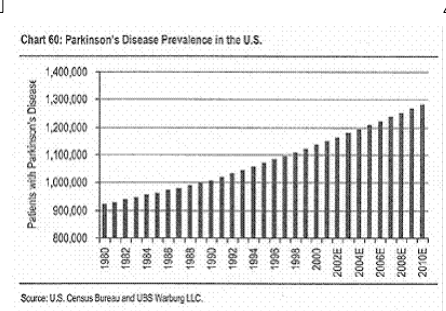
The Autism Spectrum

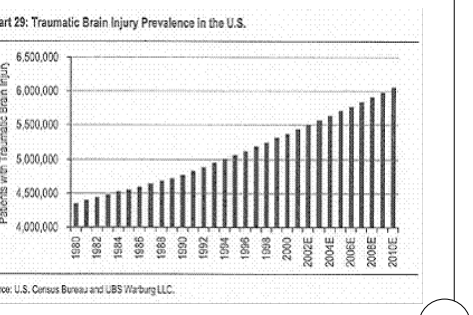
Autism Spectrum
Disorder
1/150
MMWR Feb, 2007

The Broader Autism Phenotype ???









Speech and language of parents

	Autism	Down S.
	N=46	N=55
Too detailed	11	3
Failure to reference	8	0
Vague accounts	9	2
Disorganized	11	1
Failure to clarify	12	0
Out of sync	12	0
Unusual timing	11	0
Volume abn.	9	1

Piven, 1997

Elements of autism diagnosis:

- Careful developmental history
- Program information
- Observations of the child
- Interactions with the child
- DSM-IV criteria
- Other available tools (e.g., ADOS)
- Look for clues to medical diagnosis
- Explanation of the diagnostic process
- Documentation of thought processes

Two Levels of Diagnosis

- Developmental Diagnosis
  - How do we describe this developmental pathway?
    - Autism, MR/CD, LD, ADHD, CP
- Medical Cause
  - What caused this?
    - Specific syndromes or events

Never mistake a developmental diagnosis with a causative medical condition

- There are hundreds of rare or uncommon medical causes of DD
- *Knowing* the cause does not change the educational approach to a child
- *Not knowing* the cause does not change the educational approach to a child

DSM-IV Criteria

Social Criteria (4)	Communication Criteria (4)
Behavioral Criteria (4)	4/12 = PDD-NOS 6/12 = Autism

DSM-IV: Social Criteria

- Qualitative impairment in social interaction, as manifested by 2 of:
  - Marked impairment in use of multiple nonverbal behaviors to regulate social interaction
  - Failure to develop peer relationships appropriate to developmental level
  - Lack of spontaneous seeking to share enjoyment, experiences with others
  - Lack of social or emotional reciprocity

DSM-IV: Communication

- Qualitative impairments manifested by at least one:
  - Delay/lack of development of spoken language, without adequate compensation
  - Impairment in ability to initiate or sustain a conversation with others
  - Stereotyped and repetitive use of language
  - Lack of varied, spontaneous make-believe play or social imitative play, appropriate to development

DSM-IV: Behavioral Criteria

- Restricted, repetitive and stereotyped patterns of behavior, interests and activities, manifested by at least one:
  - Encompassing preoccupation with one or more stereotyped and restricted pattern of interest, abnormal in intensity or focus
  - Inflexible adherence to specific nonfunctional routines or rituals
  - Stereotyped, repetitive motor mannerisms
  - Persistent preoccupation with parts of objects

These characteristics have to have a functional impact on life of the child.

Onset of recognized symptoms should develop before 3 years of age.

Sometimes it takes a minute to identify autism; sometimes it can take hours.

Positive Signs of Autism

- Hand-flapping
- Other repetitive behaviors
- Toe walking
- Lining up toys
- High-pitched vocalizations

Negative Signs of Autism

- Limitation of:
  - Eye contact
  - Gestures
  - Social Greetings
  - Pretend Play
  - Language
  - Peer play
  - Joint attention

All behaviors must be interpreted in the context of a child's developmental level.

Intelligence tests (IQ) are still important in the evaluation of children with developmental delays.

Intelligence Tests

- Designed to find children who needed special education
- May not show a child's BEST performance, but how s/he compares to other children the same age in the same situation
- Predicts academic success
- Stability emerges @ 6-8 years

Synonyms for MR

- Global developmental delays (medically correct label, foreshadows MR diagnosis
- Cognitive Disability (educational)
- Intellectual Disability (current literature)
- Mental retardation (old, most stigmatizing AND the most meaningful

MR Terms Confusing

- The educational categories of CD-B and CD-S confound the categories of MR established by psychologists
- The term "borderline" has a specific meaning, an IQ between 70-80. Educationally, it targets children with mild MR (IQ 55-70).
- Parents think their child has a "mild" or "borderline" problem, which is not at all what we really mean

History of Diagnosing Autism

- "Feral," "possessed," "changelings"
- 1943-44: Kanner and Asperger
- 1945-75: Psychodynamic period
- 1950-70: Only "classic" autism dx'd
- 1970-1980: Brain-based, MR, epilepsy
- 1980: "PDD" term introduced
- 1994: Asperger Syndrome
- 2000's: Focus on impaired reciprocity
  - » *Summary of talk by Isabelle Rapin, Johns Hopkins, 2006*

Personal History of Diagnosing Autism

- 1970's: The "chill up your spine" era
- 1980's: The "it's just a splinter skill" era
- 1990's-2000's: "Social reciprocity" and "joint attention" era
- Current: Diagnosing for services

Prevalence Data: Diagnostic Substitution

- Shattuck, P: The Contribution of Diagnostic Substitution to the Growing Administrative Prevalence of Autism in US Special Education, Pediatrics, 2006
- School numbers much lower than expected overall
- Educational autism is up, MR/LD down

How do we know what we know?

- The Scientific Method:
  - Make observations, organize them
  - Draw conclusions
  - Develop a hypothesis
  - Design an experiment to test the hypothesis
  - Gather data
  - If data don't fit, revise hypothesis

How do we know what we know?

- I have no truth about autism--I have accumulated evidence
- Science is a human endeavor, but it is the best way we have of figuring out the causes of and effective treatments for people with autism and their families.

"Reality is that which, when you stop believing in it, doesn't go away."

-PDK

What causes autism?

The Big Picture

Maternal Exposures

DNA----->  -----> Birth

Fetal Life

What Causes Autism?

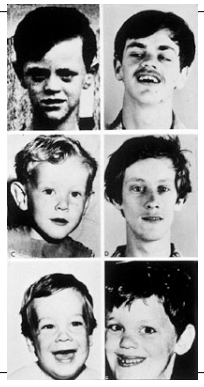
- Genetic Clues:
  - Identical twins--90% both on the spectrum
  - Fraternal twins--5-25% both on spectrum
  - Siblings--5% for autism, 10% S/L or spectrum issues
  - The Broader Autism Phenotype

What causes autism?

- Single gene or chromosomal disorders:
  - Tuberous Sclerosis
  - Smith-Magenis Syndrome
  - Smith-Lemli-Opitz
  - Rett Syndrome
  - Metabolic disorders
  - Angelman Syndrome
  - Fragile X syndrome

Fragile X Syndrome

- The most common INHERITED cause of mental retardation
- Classical features (long face, large head, large testes) not usually present in first few years of life.
- Important to test first affected child early to give family planning information.



Rett Syndrome

- The only PDD with specific test.
- Vast majority are girls.
- More profound loss of skills.
- NOT neurodegenerative
- 96% due to MECP2 mutation
- Classical phenotype by 2-3 years.

What causes autism?

- Autism and "15q"
  - 15q duplications associated with autism
  - These are inherited from the mother
  - May be more common than fragile X as a cause of autism
  - May not have been seen on chromosome analysis

What causes autism?

- What else happens between conception and birth that could cause autism?
  - Infections: Maternal rubella, CMV
  - Exposures: Thalidomide
    - Maternal antibodies
    - Other drugs?
  - Fetal stress?

What does not cause autism?

- IMMUNIZATIONS
- REFRIDGERATOR MOTHERS
- Insufficient evidence for:
  - Dietary "toxins"
  - Other heavy metal poisoning
  - Prenatal folic acid
  - Impaired "oxygenation"

Newer Ideas: Causes

- Developmental disruption disorder
- Mirror neuron dysfunction
- New candidate genes: PTEN possibly abnormal in autism with macrocephaly

The capacity for autism is present at birth

- Karin Nelson reported elevated neurotrophins and neuropeptides in cord blood of children who go on to have DD (2001)
- Tannenbaum reported abnormal movement patterns in first year
- Autism can be diagnosed on videotapes of 1st birthday parties
- Siblings of children with autism may show differences at 4 months, more clearly by 12m

Development is the result of biology and experience interacting and unfolding over time.

The Status of Early Diagnosis

- Can be suspected in infancy, but DSM-IV not helpful
- More severe the symptoms, the earlier the possible diagnosis
- There is no screening tool validated on the general population and autism does not meet generally accepted criteria for population-based screening
- Some children don't demonstrate enough diagnostic symptoms until 2 1/2-3 years

Absolute Indicators for an Autism Evaluation

- No babbling by 12 months
- No pointing or other gestures by 12m
- No single words by 16 months
- No 2-word spontaneous phrases by 24
- ANY loss of ANY language or social skill at ANY age.

» *Filipek, et al, 1999*

"ADOS": Autism Diagnostic Observation Schedule

- Developed by Cathy Lord, PhD, et al
- Cleverly designed activities to elicit autistic characteristics
- Standardized assessment tool
- 4 Modules: Nonverbal toddler to verbally fluent adolescent or adult
- Used for research or clinical purposes
- Will be increasingly needed to document diagnostic process

Stability of Diagnosis

- Most children who receive a diagnosis of an autistic spectrum disorder stay on the spectrum
- Rarely, a child will "fall off" the spectrum
- Children may move across PDD categories over time
- Current long term prognosis is poor, but not based on children who have had intensive, early intervention

Complex Diagnostics

- Reactive attachment disorder
- Bipolar disorder
- Obsessive Compulsive Disorder
- Generalized anxiety disorder
- Oppositional Defiant Disorder/Conduct Disorder
- ADHD

Effectiveness of Early Intervention

- Howlin P, J Neural Transmission (2005)
- Sallow and Graupner, AJMR, 2005: replicated Lovaas results
- Studies not uniformly positive
- Results not unique to autism (intensive and enthusiastic work can promote positive development in any developmental disorder)

Alternative Treatments

- Every parent wants to feel as if they have done everything possible.
- Non-evidence-based treatments can waste time, energy and money.
- We can't afford to spend family resources and tax dollars on avenues that are not likely to produce results.
- We can't waste our children's time.

Interventions that do not cure autism:

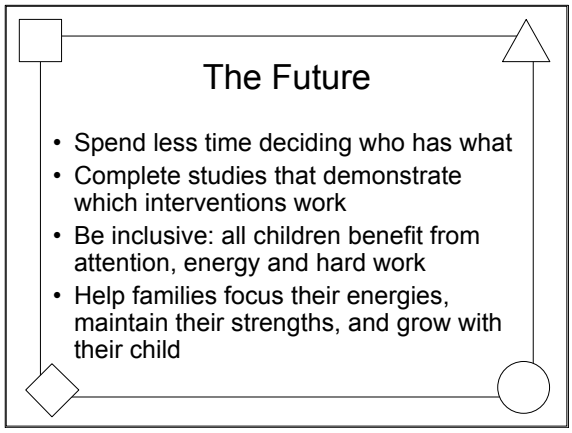
- Secretin
- Facilitated communication
- Chelation
- Antitestosterone therapy
- Hyperbaric oxygen

"Science is what we have learned about how to keep from fooling ourselves."

-Richard Feynman, physicist

Medical Diagnostics

- Audiometric exam
- Lead level for mouthing
- Disorder of form (dysmorphology)
  - High resolution chromosomes
  - Molecular fragile X testing
  - 15q microduplication studies
  - PTEN mutation testing with macrocephaly?
- Disorder of function (neurology)
  - EEG if symptoms of seizures or regression
  - MRI scan for abnormal exam, macrocephaly


The Future
• Spend less time deciding who has what
• Complete studies that demonstrate which interventions work
• Be inclusive: all children benefit from attention, energy and hard work
• Help families focus their energies, maintain their strengths, and grow with their child